

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.  
530 Virginia Road, P.O. Box 9133  
Concord, MA 01742-9133

Telephone: (978) 341-0036

Facsimile: (978) 341-0136

**UNOFFICIAL DOCUMENT FOR EXAMINER'S REVIEW**

**FACSIMILE COVER SHEET**

**Examiner:** Janet L. Epps-Ford

**Group:** 1635

RECEIVED  
CENTRAL FAX CENTER

JUN 16 2004

**Date:** June 16, 2004

**Client Code:** 2719

**Facsimile No.:** (571)273-0757

OFFICIAL

**From:** Jesse A. Fecker

**Subject: Paper:** Pending Claims

**Docket No.:** 2719.2017-001

**Applicants:** Glenn McGall, *et al.*

**Serial No.:** 09/810,434

**Filing Date:** March 15, 2001

Number of pages including this cover sheet: 5

Please confirm receipt of facsimile: Yes X No     

**Comments:**

Attached are the pending claims for the above-referenced application. Please call me if we can supply any further information.

Privileged and Confidential - All information transmitted hereby is intended only for the use of the addressee(s) named above. If the reader of this message is not the intended recipient or the employee or agent responsible for delivering the message to the intended recipient(s), please note that any distribution or copying of this communication is strictly prohibited. Anyone who received this communication in error is asked to notify us immediately by telephone and to destroy the original message or return it to us at the above address via first class mail.

LMT/JAI/rm  
@PFDesktop\::ODMA/MIODMA/HBSR05;iManage;468648;1

2719.2017-001

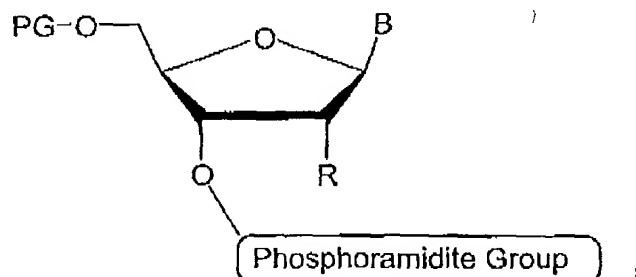
## CLAIMS AS AMENDED 3/10/03

1. (Previously presented) A method of oxidizing a phosphite ester linkage in a nucleic acid array to a phosphate linkage, comprising contacting said phosphite ester linkage with a solution of from about 0.005 M to about 0.05 M iodine in a mixture of water and organic solvent to form said phosphate linkage.
2. (Previously presented) A method of synthesizing a nucleic acid array on a support, wherein each nucleic acid occupies a separate known region of the support, said synthesizing comprising:
  - (a) activating a region of the support;
  - (b) attaching a nucleotide to a first region, said nucleotide having a masked reactive site linked to a protecting group;
  - (c) repeating steps (a) and (b) on other regions of said support whereby each of said other regions has bound thereto another nucleotide comprising a masked reactive site link to a protecting group, wherein said another nucleotide may be the same or different from that used in step (b);
  - (d) removing the protecting group from one of the nucleotides bound to one of the regions of the support to provide a region bearing a nucleotide having an unmasked reactive site;
  - (e) binding an additional nucleotide to the nucleotide with an unmasked reactive site;
  - (f) repeating step (d) and (e) on regions of the support until a desired plurality of nucleic acids is synthesized, each nucleic acid occupying separate known regions of the support;wherein said attaching and said binding are each made by covalently forming a phosphite triester linkage between said nucleotides and said unmasked reactive site and further comprising oxidizing said phosphite triester linkage to a phosphate triester linkage

with a solution of from about 0.005 M to about 0.05 M iodine in an aqueous solvent mixture.

3. (Previously presented) A method in accordance with Claim 2, wherein said synthesizing comprises the sequential steps of:
  - (a) removing a photoremoveable protecting group from at least a first area of a surface of a substrate, said surface comprising immobilized nucleotides on said surface, said nucleotides capped with a photoremoveable protecting group, without removing a photoremoveable protecting group from at least a second area of said surface;
  - (b) simultaneously contacting said first area and said second area of said surface with a first nucleotide to couple said first nucleotide to said immobilized nucleotides in said first area, and not in said second area, said first nucleotide capped with said photoremoveable protecting group;
  - (c) removing a photoremoveable protecting group from at least a part of said first area of said surface and at least a part of said second area;
  - (d) simultaneously contacting said first area and said second area of said surface with a second nucleotide to couple said second nucleotide to said immobilized nucleotides in at least a part of said first area and at least a part of said second area;
  - (e) performing additional removing and nucleotide contacting and coupling steps so that a matrix array of at least 100 nucleic acids having different sequences is formed on said support;with the proviso that the coupling steps further comprise oxidizing an initially formed phosphite ester linkage to a phosphate ester linkage using from about 0.005 M to about 0.05 M iodine in an aqueous solvent mixture.
4. (Original) A method in accordance with Claim 3, wherein said aqueous solvent mixture comprises iodine in an amount of about 0.02 M.

5. (Previously presented) A method in accordance with Claim 3, wherein said nucleotides have the formula:



wherein

B is a member selected from the group consisting of natural or unnatural adenine, natural or unnatural guanine, natural or unnatural thymine, natural or unnatural cytosine, and natural or unnatural uracil;

R is a member selected from the group consisting of hydrogen, hydroxy, protected hydroxy, halogen and alkoxy; and

PG is a photoremovable protecting group.

6. (Original) A method in accordance with Claim 5, wherein B is selected from the group consisting of adenine, guanine, cytosine and thymine and R is hydrogen.
7. (Original) A method in accordance with Claim 5, wherein said array comprises at least 10 different nucleic acids.
8. (Original) A method in accordance with Claim 5, wherein said array comprises at least 100 different nucleic acids.
9. (Original) A method in accordance with Claim 5, wherein said array comprises at least 1000 different nucleic acids.
10. (Original) A method in accordance with Claim 5, wherein said array comprises at least 10,000 different nucleic acids.

11. (Original) A method in accordance with Claim 5, wherein said array comprises at least 100,000 different nucleic acids.
12. (Original) A method in accordance with Claim 5, wherein each different nucleic acid is in a region having an area of less than about 1 cm<sup>2</sup>.
13. (Original) A method in accordance with Claim 5, wherein each different nucleic acid is in a region having an area of less than about 1 mm<sup>2</sup>.
14. (Original) A method in accordance with Claim 5, wherein said solution is about 0.02 M iodine in a mixture of water, pyridine and THF.
15. (Original) A method in accordance with Claim 5, wherein B is selected from the group consisting of adenine, guanine, cytosine and thymine, R is hydrogen, and said solution is about 0.02 M iodine in a mixture of water, pyridine and THF.
16. (Original) A method in accordance with Claim 5, wherein B is selected from the group consisting of adenine, guanine, cytosine and thymine, R is hydrogen, PG is McNPOC and said solution is about 0.02 M iodine in a mixture of water, pyridine and THF.
17. (Previously Presented) A method in accordance with Claim 5, wherein B is selected from the group consisting of adenine, guanine, cytosine and thymine, R is hydrogen, PG is McNPOC, the phosphoramidite group is -P(OCH<sub>2</sub>CH<sub>2</sub>CN)N(iPr)<sub>2</sub> and said solution is about 0.02 M iodine in a mixture of water, pyridine and THF.
18. (Previously Presented) The method of Claim 5, wherein from about 0.01 M to about 0.05 M iodine is present in the aqueous solvent mixture.
19. (Previously Presented) The method of Claim 18, wherein from about 0.02 M to about 0.05 M iodine is present in the aqueous solvent mixture.